

CLAIMS

1. A method of treating tumors in a subject in need of such treatment, comprising the following steps:

(A) administering a tumor-treating effective amount of an agent to the subject, wherein the agent comprises

(a) 5-chloro-2'-deoxycytidine without a cytidine deaminase inhibitor, 5-fluoro-2'-deoxycytidine (FdC), 5-fluoro-2'-deoxyuridine (FdU), and N-(phosphonacetyl)-L-aspartate (PALA), wherein 5-chloro-2'-deoxycytidine enhances the incorporation of a radiosensitizing metabolite of 5-chloro-2'-deoxycytidine into DNA, precluding the need for administering an inhibitor for the formation of TTP,

(b) 5-chloro-2'-deoxycytidine and a cytidine deaminase inhibitor, without 5-fluoro-2'-deoxycytidine (FdC), 5-fluoro-2'-deoxyuridine (FdU), and N-(phosphonacetyl)-L-aspartate (PALA), wherein 5-chloro-2'-deoxycytidine enhances the incorporation of a radiosensitizing metabolite of 5-chloro-2'-deoxycytidine into DNA, precluding the need for administering an inhibitor for the formation of TTP,

(c) 5-chloro-2'-deoxycytidine and 4-N-methylamino FdC, or

(d) 5-chloro-2'-deoxycytidine, 4-N-methylamino FdC and a cytidine deaminase inhibitor; and

(B) exposing the subject to a tumor-treating effective amount of radiation.

2. The method of claim 1, wherein said agent is administered in a slow release formulation.

3. The method of claim 1, wherein the cytidine deaminase inhibitor is tetrahydrouridine, deoxytetrahydrouridine, a pyrimidin-2-one nucleoside, a F pyrimidin-2-one nucleoside, a diazepin-2-1-nucleoside, 1-(2-Deoxy-2-fluoro- β -D arabinofuranosyl)-1,2-dihydropyrimidin-2-one, 2'-Deoxy-2'-F-arazebularine, diazoepinone, 4-hydromethyl-2-oxopyrimidin-2-one nucleoside, or 2'-fluoro-2'-deoxyarabinosyl-tetrahydrouracil.

4. The method of claim 3, wherein said pyrimidin-2-one nucleoside is 1- β -ribofuranocyl-1,2-dihydropyrimidin-2-one (Zebularine) or 5-fluoro-pyrimidin-2-one-nucleoside.

5. The method of claim 4, wherein the cytidine deaminase inhibitor is tetrahydrouridine or Zebularine.

6. The method of claim 5, wherein the cytidine deaminase inhibitor is tetrahydrouridine.

7. The method of claim 1, wherein said subject is a human.

8. The method of claim 1, wherein the radiation is selected from the group consisting of radiation from protons as a radiation source, radiation from a radiation source implanted proximal to the tumor, radiation from a radionuclide attached to monoclonal antibodies, radiation in a gamma knife, 3D conformal radiation, and radiation in steriotactic radiosurgery.

9. The method of claim 8, wherein said radiation source implanted proximal to the tumor comprises yttrium 90 needles or iridium needles.

10. The method of claim 8, wherein said radionuclide is yttrium 90.
11. The method of claim 1, further comprising administering bisulfite to the subject before exposing the subject to radiation.
12. The method of claim 11, further comprising administering cysteine to the subject before exposing the subject to radiation.
13. The method of claim 1, further comprising exposing the subject to radiation before step (A).
14. A method of hypomethylating genes in a subject in need of such hypomethylation, comprising administering a gene-hypomethylating effective amount of an agent to the subject, wherein said agent comprises
- (a) 5-chloro-2'-deoxycytidine without a cytidine deaminase inhibitor,
 - (b) 5-chloro-2'-deoxycytidine and a cytidine deaminase inhibitor,
 - (c) 5-chloro-2'-deoxycytidine and 4-N-methylamino FdC, or
 - (d) 5-chloro-2'-deoxycytidine, 4-N-methylamino FdC and a cytidine deaminase inhibitor.
15. The method of claim 14, wherein the cytidine deaminase inhibitor is tetrahydrouridine, deoxytetrahydrouridine, a pyrimidin-2-one nucleoside, a F pyrimidin-2-one

nucleoside, a diazepin-2-1-nucleoside, 1-(2-Deoxy-2-fluoro- β -D arabinofuranosyl)-1,2-dihydropyrimidin-2-one, 2'-Deoxy-2'-F-arazebularine, diazoepinone, 4-hydromethyl-2-oxypyrimidin-2-one nucleoside, or 2'-fluoro-2'-deoxyarabinosyl-tetrahydrouracil.

16. The method of claim 15, wherein said pyrimidin-2-one nucleoside is 1- β -riboduranocyl-1,2-dihydropyrimidin-2-one (Zebularine) or 5-fluoro-pyrimidin-2-one-nucleoside.

17. The method of claim 16, wherein the cytidine deaminase inhibitor is tetrahydrouridine or Zebularine.

18. The method of claim 17, wherein the cytidine deaminase inhibitor is tetrahydrouridine.

19. The method of claim 14, wherein said subject is a human.

20. The method of claim 14, further comprising exposing the subject to a tumor-treating effective amount of radiation, wherein the agent hypomethylates genes silenced in a tumor to reduce (A) the aggressiveness of the tumor, (B) the metastatic propensity of the tumor, (C) the genetic instability of the tumor, and/or (D) the resistance of the tumor to drug or radiation treatment.

21. A pharmaceutical composition comprising 5-chloro-2'-deoxycytidine and 4-N-methylamino FdC.